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| | | | |
|---|---|---|---|
| NEWS | 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS | 2 | | "Ask CAS" for self-help around the clock |
| NEWS | 3 | JAN 17 | Pre-1988 INPI data added to MARPAT |
| NEWS | 4 | FEB 21 | STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results |
| NEWS | 5 | FEB 22 | The IPC thesaurus added to additional patent databases on STN |
| NEWS | 6 | FEB 22 | Updates in EPFULL; IPC 8 enhancements added |
| NEWS | 7 | FEB 27 | New STN AnaVist pricing effective March 1, 2006 |
| NEWS | 8 | MAR 03 | Updates in PATDPA; addition of IPC 8 data without attributes |
| NEWS | 9 | MAR 22 | EMBASE is now updated on a daily basis |
| NEWS | 10 | APR 03 | New IPC 8 fields and IPC thesaurus added to PATDPAFULL |
| NEWS | 11 | APR 03 | Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL |
| NEWS | 12 | APR 04 | STN AnaVist $500 visualization usage credit offered |
| NEWS | 13 | APR 12 | LINSPEC, learning database for INSPEC, reloaded and enhanced |
| NEWS | 14 | APR 12 | Improved structure highlighting in FQHIT and QHIT display in MARPAT |
| NEWS | 15 | APR 12 | Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected |
| NEWS | 16 | MAY 10 | CA/CAplus enhanced with 1900-1906 U.S. patent records |
| NEWS | 17 | MAY 11 | KOREAPAT updates resume |
| NEWS | 18 | MAY 19 | Derwent World Patents Index to be reloaded and enhanced |

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/

| | |
|---|---|
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |
| NEWS X25 | X.25 communication option no longer available after June 2006 |

Enter NEWS followed by the item number or name to see news on that specific topic.

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**COMPLETE THE STN SURVEY - APRIL 27 THROUGH MAY 31**

**Dear valued STN customer,**

**In an effort to enhance your experience with STN, we would like to better understand what you find useful. Please take approximately 5 minutes to complete a web survey.**

**If you provide us with your name, login ID, and e-mail address, you will be entered in a drawing to win a free iPod(R). Your responses will be kept confidential and will help us make future improvements to STN.**

**Take survey: http://www.zoomerang.com/survey.zgi?p=WEB2259HNKWTUW**

**Thank you in advance for your participation.**

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:39:19 ON 26 MAY 2006

=> FILE REG

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 12:39:23 ON 26 MAY 2006
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 MAY 2006 HIGHEST RN 885654-58-0
DICTIONARY FILE UPDATES: 25 MAY 2006 HIGHEST RN 885654-58-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

**********************************************************
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
**********************************************************

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

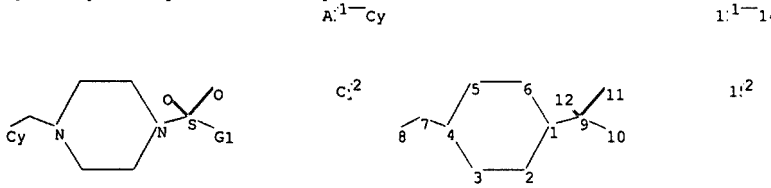
=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=>

STN SEARCH TRANSCRIPT 10/681,205

Uploading C:\Program Files\Stnexp\Queries\HABTE SULFONYL RCE.str



chain nodes :
7 8 9 10 11 12 13 14 15
ring nodes :
1 2 3 4 5 6
chain bonds :
1-9 4-7 7-8 9-10 9-11 9-12 13-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 1-9 2-3 3-4 4-5 4-7 5-6 7-8 9-10 9-11 9-12 13-14
isolated ring systems :
containing 1 :

G1:[*1],[*2]

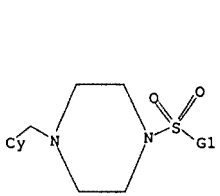
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:Atom 15:Atom
Generic attributes :
8:
Type of Ring System : Polycyclic
13:
Saturation : Unsaturated
14:
Saturation : Unsaturated
Type of Ring System : Polycyclic
15:
Type of Ring System : Polycyclic

L1 STRUCTURE UPLOADED

=> que L1

L2 QUE L1

=> D L1
L1 HAS NO ANSWERS
L1 STR



G1 [@1],[@2]

Structure attributes must be viewed using STN Express query preparation.

=> S L1
SAMPLE SEARCH INITIATED 12:39:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2567 TO ITERATE

77.9% PROCESSED 2000 ITERATIONS 42 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 48301 TO 54379
PROJECTED ANSWERS: 638 TO 1518

L3 42 SEA SSS SAM L1

=> FILE CAPLUS

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.44 | 0.65 |

FILE 'CAPLUS' ENTERED AT 12:39:45 ON 26 MAY 2006
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FILE COVERS 1907 - 26 May 2006 VOL 144 ISS 23
FILE LAST UPDATED: 25 May 2006 (20060525/ED)

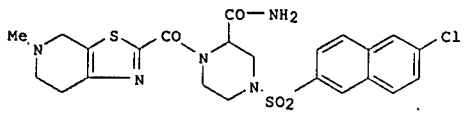
Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> S L3
L4 10 L3

=> D 1-10 IBIB ABS HITSTR

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:64500 CAPLUS
DOCUMENT NUMBER: 144:205149
TITLE: Design, synthesis, and biological activity of novel factor Xa inhibitors: Improving metabolic stability by S1 and S4 ligand modification
AUTHOR(S): Komoriya, Satoshi; Kobayashi, Shozo; Osanai, Ken; Yoshino, Toshiharu; Nagata, Tsutomu; Haginoya, Noriyasu; Nakamoto, Yumi; Mochizuki, Akiyoshi; Nagahara, Takayasu; Suzuki, Makoto; Shimada, Takashi; Watanabe, Kengo; Isobe, Yumiko; Furugoori, Taketoshi
CORPORATE SOURCE: Tokyo R&D Center, Daiichi Pharmaceutical Co. Ltd, 16-13, Kita-Kasai 1-Chome, Edogawa-ku, Tokyo, 134-8630, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(5), 1309-1330
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

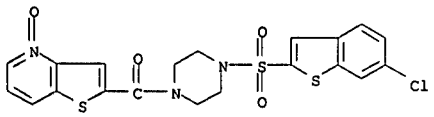


I

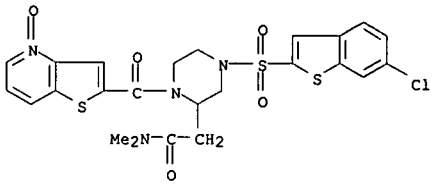
AB Serine protease factor Xa (fXa) inhibitor I showed good ex vivo anti-fXa activity upon oral administration in rats. However, it has been revealed that I had low metabolic stability against human liver microsomes. To improve the metabolic stability, we attempted to modify the S1 and S4 ligands of I. These modifications resulted in a compound which exhibited selective anti-fXa activity and excellent anti-coagulation activity.

IT **875573-53-8P 875573-54-9P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(factor Xa inhibitors with improved metabolic stability)

RN 875573-53-8 CAPLUS
CN Piperazine, 1-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-4-[(4-oxidothieno[3,2-b]pyridin-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

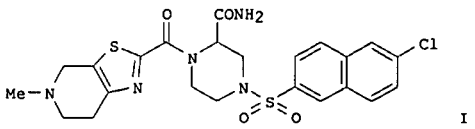


RN 875573-54-9 CAPLUS
CN 2-Piperazineacetamide, 4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-N,N-dimethyl-1-[(4-oxidothieno[3,2-b]pyridin-2-yl)carbonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:747454 CAPLUS
DOCUMENT NUMBER: 141:395464
TITLE: Synthesis and Conformational Analysis of a Non-Amidine Factor Xa Inhibitor That Incorporates 5-Methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine as S4 Binding Element
AUTHOR(S): Haginoya, Noriyasu; Kobayashi, Syozo; Komoriya, Satoshi; Yoshino, Toshiharu; Suzuki, Makoto; Shimada, Takashi; Watanabe, Kengo; Hirokawa, Yumiko; Furugori, Taketoshi; Nagahara, Takayasu
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co. Ltd, Edogawa-ku, Tokyo, 134-8630, Japan
SOURCE: Journal of Medicinal Chemistry (2004), 47(21), 5167-5182
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:395464
GI



I

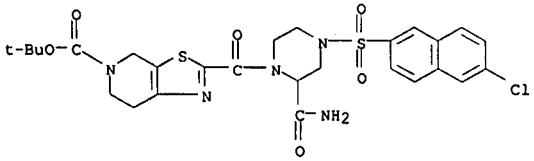
AB Our exploratory study was based on the concept that a non-amidine factor Xa (fXa) inhibitor is suitable for an orally available anticoagulant. We synthesized and evaluated a series of N-(6-chloronaphthalen-2-yl)sulfonylpiperazine derivs. incorporating various fused-bicyclic rings containing an aliphatic amine expected to be S4 binding element. Among this series, 5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine type I displayed orally potent anti-fXa activity and evident prolongation of prothrombin time (PT) with the moderate bioavailability in rats. The X-ray crystal anal. afforded an obvious binding mode that

5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine and 6-chloronaphthalene resp. bound to S4 and S1 subsites. In this X-ray study, we discovered a novel intramol. S-O close contact. Ab initio energy calcns. of model compds. deduced that conformers with the most close S-O proximity were most stable. The Mulliken population anal. proposed that this energy profile was caused by both of electrostatic S-O affinity and N-O repulsion. The results of these calcns. and X-ray anal. suggested a possibility that the restricted conformation effected the affinity to S4 subsite of fXa.

IT **222987-45-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, factor Xa inhibition activity and structure-activity relationship of (chloronaphthalenylsulfonyl)piperazines bearing fused-heterobicyclic rings)

RN 222987-45-3 CAPLUS

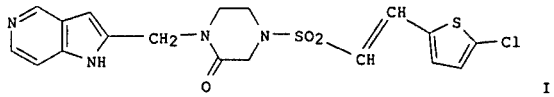
CN Thiazolo[5,4-c]pyridine-5(4H)-carboxylic acid, 2-[[2-(aminocarbonyl)-4-[(6-chloro-2-naphthalenyl)sulfonyl]-1-piperazinyl]carbonyl]-6,7-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:89919 CAPLUS
DOCUMENT NUMBER: 138:247939
TITLE: Discovery of an orally efficacious inhibitor of coagulation factor Xa which incorporates a neutral P1 ligand
AUTHOR(S): Choi-Sledeski, Yong Mi; Kearney, Robert; Poli, Gregory; Pauls, Henry; Gardner, Charles; Gong, Yong; Becker, Michael; Davis, Roderick; Spada, Alfred; Liang, Guyan; Chu, Valeria; Brown, Karen; Collussi, Dennis; Leadley, Robert, Jr.; Rebello, Sam; Moxey, Phillip; Morgan, Suzanne; Bentley, Ross; Kasiewski, Charles; Maignan, Sebastien; Guilloteau, Jean-Pierre; Mikol, Vincent
CORPORATE SOURCE: Department of Medicinal Chemistry, Aventis Pharmaceuticals, Bridgewater, NJ, 08807-0800, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(5), 681-684
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:247939
GI



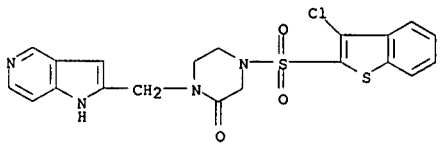
I

AB The discovery and SAR of ketopiperazino methylazaindole factor Xa inhibitors are described. Structure-activity data suggesting that this class of inhibitors does not bind in the canonical mode were confirmed by an X-ray crystal structure showing the neutral haloarom. bound in the S1 subsite. The most potent azaindole (I, RPR209685) is selective against related serine proteases and attains higher levels of exposure upon oral dosing than comparable benzamidines and benzamidine isosteres. Compound I was efficacious in the canine AV model of thrombosis.

IT **234100-32-4P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(discovery of an orally efficacious inhibitor of coagulation factor Xa which incorporates a neutral P1 ligand)

RN 234100-32-4 CAPLUS

CN Piperazinone, 4-[(3-chlorobenzo[b]thien-2-yl)sulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:769282 CAPLUS
DOCUMENT NUMBER: 135:313616
TITLE: Heterocyclic sulfonyl compounds and activated blood coagulation factor X (FXa) inhibitors containing them
INVENTOR(S): Kobayashi, Shozo; Komoritani, Satoshi; Haginoya, Noriyasu; Suzuki, Masanori; Yoshino, Toshiharu; Nagahara, Takayasu; Yoshikawa, Kenji; Muto, Akira; Ozanai, Takeshi; Nakamoto, Yumi; Mochizuki, Akiyoshi; Nagata, Tsutomu
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 304 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2001294572 | A2 | 20011023 | JP 2000-38100 | 20000209 |

PRIORITY APPLN. INFO.: JP 2000-38100 20000209
OTHER SOURCE(S): MARPAT 135:313616

AB Pharmaceuticals, useful for prevention and/or treatment of thrombus and embolus, contain Q1Q2T1SO2QA [I; Q1 = (un)substituted bicyclic or

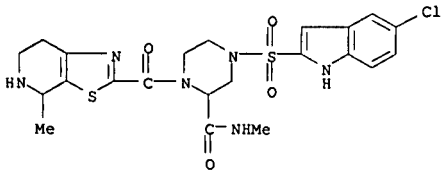
tricyclic group; Q2 = single bond, O, S, C1-6 alkylene, etc.; Q3 = N-containing cyclic group; QA = (un)substituted (hetero)arylalkenyl, bicyclic or tricyclic group, etc.; T1 = CO, (un)substituted methylene, etc.], their salts, or solvates. (2RS)-2-(N-tert-butoxycarbonylaminomethyl)-6-methoxycarbonyl-1,2,3,4-tetrahydronaphthalene was treated with NaOH, condensed with 1-[(6-chloronaphthalen-2-yl)sulfonyl]piperazine.HCl, and deprotected to give (RS)-I.HCl (Q1 = 6-aminomethyl-5,6,7,8-tetrahydronaphthalen-2-yl, Q2 = bond, T1 = CO, Q3 = 1,4-piperazinediyl, QA = 6-chloronaphthalen-2-yl). I.HCl (Q1 = 5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl, Q2 = bond, T1 = CO, Q3 = 1,4-piperazinediyl, QA = 6-chloronaphthalen-2-yl) in vitro inhibited human FXa with IC50 of 20 nM.

IT **259805-94-2P 259806-37-6P 259806-48-9P**
**259806-67-2P 259806-89-8P 259806-92-3P**
**259807-04-0P 368439-26-3P 368439-42-3P**
**368439-49-0P 368439-57-0P 368439-65-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic sulfonyl compds. as activated blood coagulation factor X inhibitors)

RN 259805-94-2 CAPLUS
CN 2-Piperazinecarboxamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-methyl-1-[(4,5,6,7-tetrahydro-4-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

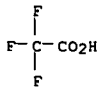
CM 1

CRN 259805-93-1
CMF C22 H25 Cl N6 O4 S2

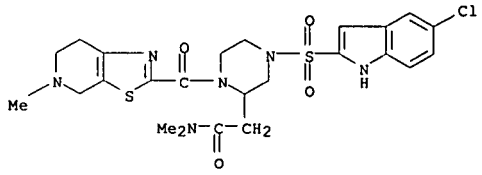


CM 2

CRN 76-05-1
CMF C2 H F3 O2

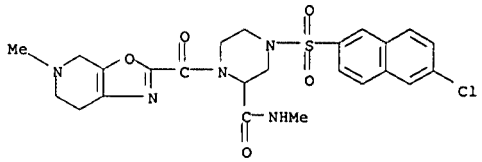


RN 259806-37-6 CAPLUS
CN 2-Piperazineacetamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N,N-dimethyl-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

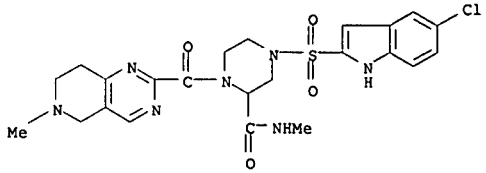


● HCl

RN 259806-48-9 CAPLUS
CN 2-Piperazinecarboxamide, 4-[(6-chloro-2-naphthalenyl)sulfonyl]-N-methyl-1-[(4,5,6,7-tetrahydro-5-methyloxazolo[5,4-c]pyridin-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

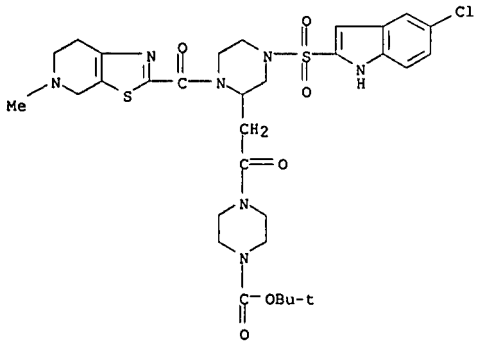


RN 259806-67-2 CAPLUS
CN 2-Piperazinecarboxamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-methyl-1-[(5,6,7,8-tetrahydro-6-methylpyrido[4,3-d]pyrimidin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

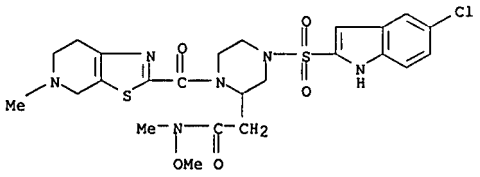


● HCl

RN 259806-89-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[(5-chloro-1H-indol-2-yl)sulfonyl]-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-2-piperazinyl]acetyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

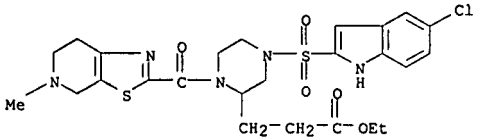


RN 259806-92-3 CAPLUS
CN 2-Piperazineacetamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-methoxy-N-methyl-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

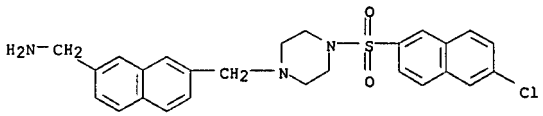


● HCl

RN 259807-04-0 CAPLUS
CN 2-Piperazinepropanoic acid, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

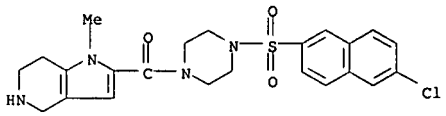


RN 368439-26-3 CAPLUS
CN Piperazine, 1-[[7-(aminomethyl)-2-naphthalenyl]methyl]-4-[(6-chloro-2-naphthalenyl)sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



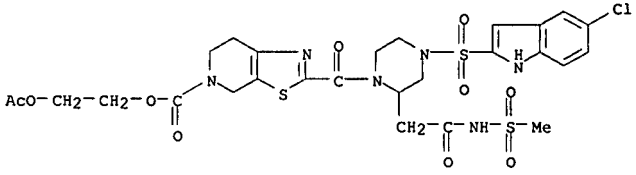
● HCl

RN 368439-42-3 CAPLUS
CN Piperazine, 1-[(6-chloro-2-naphthalenyl)sulfonyl]-4-[(4,5,6,7-tetrahydro-1-methyl-1H-pyrrolo[3,2-c]pyridin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

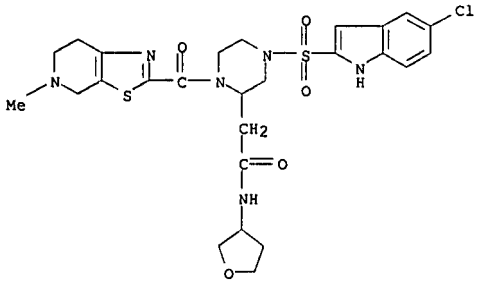


● HCl

RN 368439-49-0 CAPLUS
CN Thiazolo[5,4-c]pyridine-5(4H)-carboxylic acid, 2-[[4-[(5-chloro-1H-indol-2-yl)sulfonyl]-2-[2-[(methylsulfonyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]-6,7-dihydro-, 2-(acetyloxy)ethyl ester (9CI) (CA INDEX NAME)

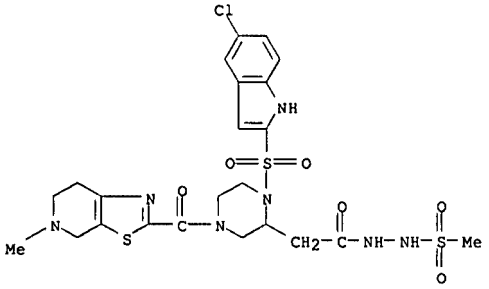


RN 368439-57-0 CAPLUS
CN 2-Piperazineacetamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-(tetrahydro-3-furanyl)-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



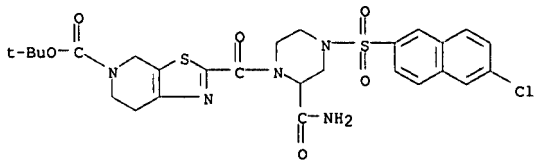
● HCl

RN 368439-65-0 CAPLUS
CN 2-Piperazineacetic acid, 1-[(5-chloro-1H-indol-2-yl)sulfonyl]-4-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, 2-(methylsulfonyl)hydrazide, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

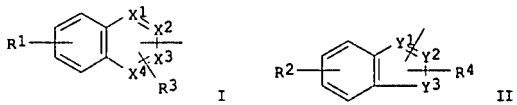
IT **222987-45-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic sulfonyl compds. as activated blood coagulation factor X inhibitors)
RN 222987-45-3 CAPLUS
CN Thiazolo[5,4-c]pyridine-5(4H)-carboxylic acid, 2-[[2-(aminocarbonyl)-4-[(6-chloro-2-naphthalenyl)sulfonyl]-1-piperazinyl]carbonyl]-6,7-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



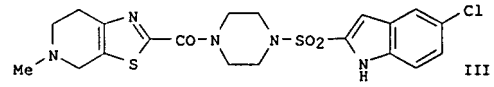
L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:636077 CAPLUS
DOCUMENT NUMBER: 135:211057
TITLE: Preparation of N-(tetrahydrothiazolo[5,4-c]pyridin-2-ylcarbonyl)piperazine derivatives and N-(4,5,6,7-tetrahydrothieno[3,2-c]pyridin-2-ylmethyl)pyrrolidine derivative and method for inhibiting trypsin-type serine proteases
INVENTOR(S): Komoriya, Satoshi; Haginoya, Noriyasu; Suzuki, Makoto
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 234 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001062763 | A1 | 20010830 | WO 2001-JP1344 | 20010223 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: JP 2000-54370 A 20000225
GI



I II



III

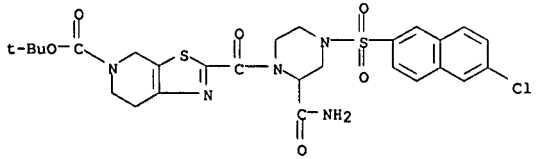
AB Trypsin-type serine protease inhibitors are compds. having groups

represented by the general formula (I) or (II) (wherein R1 and R2 are each hydrogen, C1-3 alkyl, halo, C2-3 alkenyl, or ethynyl; or R3 and R4 are each hydrogen, hydroxyl, or amino; X1, X2, X3 and X4 are each CH or N; Y1 and Y2 are each CH or N; and Y3 is NH, O or S). When such a compound is made to act on a trypsin-type serine protease, e.g. factor Xa (Fxa), the group enters the S1 pocket to thereby exert an inhibitory activity against the protease. Thus, to a solution of 400 mg 1-[(5-chloroindol-2-yl)sulfonyl]piperazine in 100 mL DMF were added 1-hydroxybenzotriazole 10.5, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride 194, lithium 5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinecarboxylate 175, and N-methylmorpholine 86.8 mg, and the resulting mixture was stirred at room temperature for 10 h to give 1-[(5-chloroindol-2-yl)sulfonyl]-4-(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-ylcarbonyl)piperazine hydrochloride (III.HCl). III.HCl showed IC50 of 0.005 μM against human FXa. X-ray crystallog. anal. of the complexes of human Gla domain-deficient β-FXa with the above compds. showed that bicyclic aromatic group (e.g. naphthalenyl) and aromatic heterocyclyl group (e.g. chloroindolyl) entered into the S1 pocket of the Fxa.

IT **222987-45-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (tetrahydrothiazolo[c]pyridinylcarbonyl)piperazine derivs. and (tetrahydrothieno[c]pyridinylmethyl)pyrrolidine derivative and method for inhibiting trypsin-type serine proteases)

RN 222987-45-3 CAPLUS

CN Thiazolo[5,4-c]pyridine-5(4H)-carboxylic acid, 2-[[2-(aminocarbonyl)-4-[(6-chloro-2-naphthalenyl)sulfonyl]-1-piperazinyl]carbonyl]-6,7-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:78383 CAPLUS

DOCUMENT NUMBER: 134:163059

TITLE: Substituted piperazinone derivatives and other oxoazaheterocyclyl compounds useful as factor Xa/IIa inhibitors

INVENTOR(S): Ewing, William R.; Becker, Michael R.; Choi-Sledeski, Yong Mi; Pauls, Heinz W.; He, Wei; Condon, Stephen M.; Davis, Roderick S.; Hanney, Barbara A.; Spada, Alfred P.; Burns, Christopher J.; Jiang, John Z.; Li, Aiwen; Myers, Michael R.; Lau, Wan F.; Poli, Gregory B.

PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products Inc., USA

SOURCE: PCT Int. Appl., 460 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

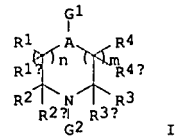
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001007436 | A2 | 20010201 | WO 2000-IB1156 | 20000726 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2382755 | AA | 20010201 | CA 2000-2382755 | 20000726 |
| BR 2000013179 | A | 20020402 | BR 2000-13179 | 20000726 |
| EP 1208097 | A2 | 20020529 | EP 2000-951781 | 20000726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| TR 200200225 | T2 | 20020621 | TR 2002-200200225 | 20000726 |
| JP 2003508353 | T2 | 20030304 | JP 2001-512520 | 20000726 |
| EE 200200045 | A | 20030616 | EE 2002-45 | 20000726 |
| AU 773227 | B2 | 20040520 | AU 2000-64628 | 20000726 |
| NO 2002000214 | A | 20020402 | NO 2002-214 | 20020115 |
| BG 106340 | A | 20021031 | BG 2002-106340 | 20020122 |
| ZA 2002000543 | A | 20030623 | ZA 2002-543 | 20020122 |

PRIORITY APPLN. INFO.: US 1999-363196 A 19990728
WO 2000-IB1156 W 20000726

OTHER SOURCE(S): MARPAT 134:163059

GI



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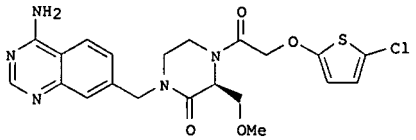
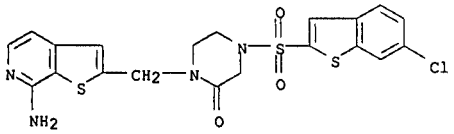


II

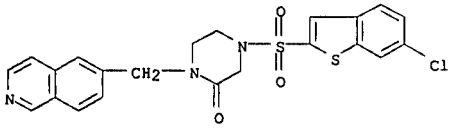
AB The invention is directed to piperazinones I and their pharmaceutically acceptable salts, prodrugs, N-oxides, hydrates, and solvates [wherein A = CH or N; G1 and G2 = L1Cy1 or L2Cy2; Cy1 and Cy2 = (un)substituted aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, etc.; L1 = null, O, S, SO, SO2, or (un)substituted sulfamoyl, methylene, (alkyl)keto(alkyl), carbamoyl, etc.; L2 = null or linking group; R1, R1a, R2, R2a, R3, R3a, R4, R4a = independently H, carboxy, alkoxycarbonyl, alkyl, (hetero)aryl, aralkyl, heteroarylalkyl, etc.; m and n = independently 0-2]. The compds. inhibit factor Xa (no data) and factor IIa, and thereby the production of thrombin, and are thus useful as anticoagulants in the treatment of a wide variety of conditions. The invention is also directed to pharmaceutical compns., synthetic intermediates, and a method of inhibiting factor Xa. Examples include the synthesis of approx. 1600 invention compds. and several hundred intermediates. For instance, condensation of 5-chloro-2-thienyloxyacetic acid with the corresponding N-benzyloxycarbonyl-protected piperazinone derivative (prepns. given), using DIPEA and TBTU in DMF, gave II.

IT **234099-55-9P 234099-62-8P 234100-32-4P**
**234100-58-4P 234105-43-2P 323587-45-7P**
**323593-63-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of piperazinone derivs. and other substituted oxoazaheterocyclyl compds. as factor Xa/IIa inhibitors)

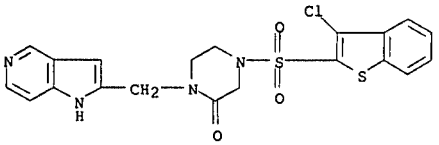
RN 234099-55-9 CAPLUS
CN Piperazinone, 1-[(7-aminothieno[2,3-c]pyridin-2-yl)methyl]-4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]- (9CI) (CA INDEX NAME)



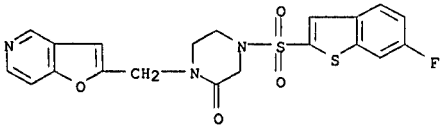
RN 234099-62-8 CAPLUS
CN Piperazinone, 4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-1-(6-isoquinolinylmethyl)- (9CI) (CA INDEX NAME)



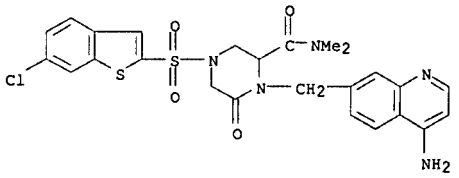
RN 234100-32-4 CAPLUS
CN Piperazinone, 4-[(3-chlorobenzo[b]thien-2-yl)sulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



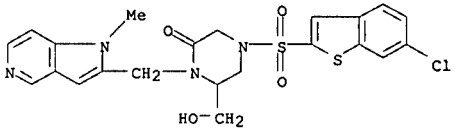
RN 234100-58-4 CAPLUS
CN Piperazinone, 4-[(6-fluorobenzo[b]thien-2-yl)sulfonyl]-1-(furo[3,2-c]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



RN 234105-43-2 CAPLUS
CN 2-Piperazinecarboxamide, 1-[(4-amino-7-quinolinyl)methyl]-4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-N,N-dimethyl-6-oxo- (9CI) (CA INDEX NAME)

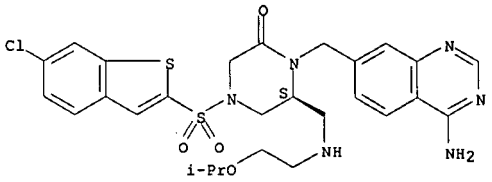


RN 323587-45-7 CAPLUS
CN Piperazinone, 4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-6-(hydroxymethyl)-1-[(1-methyl-1H-pyrrolo[3,2-c]pyridin-2-yl)methyl]- (9CI) (CA INDEX NAME)



RN 323593-63-1 CAPLUS
CN Piperazinone, 1-[(4-amino-7-quinazolinyl)methyl]-4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-6-[[[2-(1-methylethoxy)ethyl]amino]methyl]-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2000:384179 CAPLUS |
| DOCUMENT NUMBER: | 133:30741 |
| TITLE: | Substituted piperazinone derivatives and other oxoazaheterocyclyl compounds useful as factor Xa inhibitors |
| INVENTOR(S): | Ewing, William R.; Becker, Michael R.; Myers, Michael R.; Spada, Alfred P. |
| PATENT ASSIGNEE(S): | Aventis Pharmaceuticals Products Inc., USA |
| SOURCE: | PCT Int. Appl., 219 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000032590 | A1 | 20000608 | WO 1999-US28074 | 19991124 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| WO 9937304 | A1 | 19990729 | WO 1999-US1682 | 19990127 |
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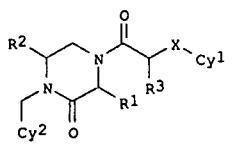
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| JP 2003529531 | T2 | 20031007 | JP 2000-585232 | 19991124 |
| PRIORITY APPLN. INFO.: | | | US 1998-110012P | A2 19981125 |
| | | | WO 1999-US1682 | A2 19990127 |
| | | | US 1999-313611 | A2 19990518 |
| | | | US 1999-363196 | A2 19990728 |
| | | | US 1998-72707P | A2 19980127 |
| | | | WO 1999-US28074 | W 19991124 |

OTHER SOURCE(S): MARPAT 133:30741
GI



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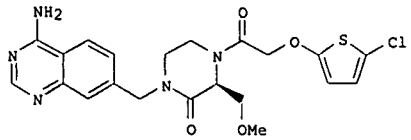
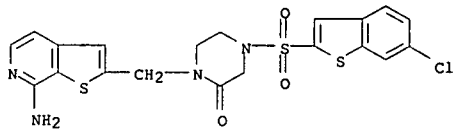


II

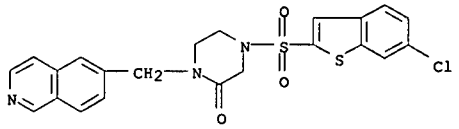
AB The invention is directed to piperazinones I and their pharmaceutically acceptable salts, prodrugs, N-oxides, hydrates, and solvates [wherein R1 = H, alkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, alkoxy, aminoalkyl, CH2OZ, CH(CH3)OZ; R2 = H, (un)substituted alkyl, aryl, aralkyl, heteroaryl, or heteroarylalkyl; R3 = H or Me; X = N or O; Z = lower alkyl or alkoxycarbonylalkyl; Cyl = (un)substituted aryl, (un)substituted heteroaryl; Cy2 = (un)substituted aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, etc.]. The compds. inhibit factor Xa (no data), and thereby the production of thrombin, and are thus useful as anticoagulants in the treatment of a wide variety of conditions. The invention is also directed to pharmaceutical compns., synthetic intermediates, and a method of inhibiting factor Xa. Examples include the synthesis of approx. 780 invention compds., approx. 50 of which are also claimed, and several hundred intermediates. For instance, condensation of 5-chloro-2-thienyloxyacetic acid with the corresponding N-benzyloxycarbonyl-protected piperazinone derivative (prepns. given), using DIPEA and TBTU in DMF, gave the preferred title compound II.

IT **234099-55-9P 234099-62-8P 234100-32-4P 234100-58-4P 234105-43-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of piperazinone derivs. and other substituted oxoazaheterocyclyl compds. as factor Xa inhibitors)

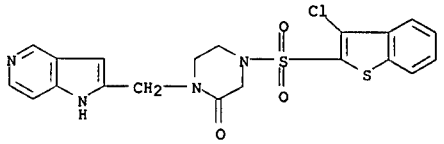
RN 234099-55-9 CAPLUS
CN Piperazinone, 1-[(7-aminothieno[2,3-c]pyridin-2-yl)methyl]-4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]- (9CI) (CA INDEX NAME)



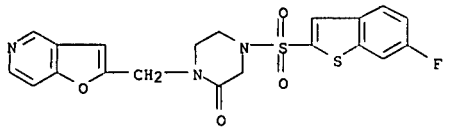
RN 234099-62-8 CAPLUS
CN Piperazinone, 4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-1-(6-isoquinolinylmethyl)- (9CI) (CA INDEX NAME)



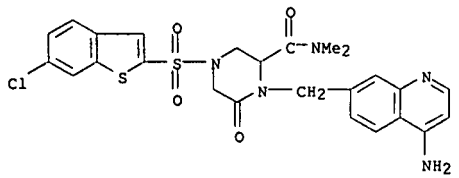
RN 234100-32-4 CAPLUS
CN Piperazinone, 4-[(3-chlorobenzo[b]thien-2-yl)sulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



RN 234100-58-4 CAPLUS
CN Piperazinone, 4-[(6-fluorobenzo[b]thien-2-yl)sulfonyl]-1-(furo[3,2-c]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



RN 234105-43-2 CAPLUS
CN 2-Piperazinecarboxamide, 1-[(4-amino-7-quinolinyl)methyl]-4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-N,N-dimethyl-6-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:133658 CAPLUS
DOCUMENT NUMBER: 132:194391
TITLE: Preparation of sulfonyl moiety-containing heterocyclic compounds as factor Xa inhibitors
INVENTOR(S): Kobayashi, Syozo; Komoriya, Satoshi; Haginoya, Noriyasu; Suzuki, Masanori; Yoshino, Toshiharu; Nagahara, Takayasu; Nagata, Tsutomu; Horino, Haruhiko; Ito, Masayuki; Mochizuki, Akiyoshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 883 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

APPLICANTS

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000009480 | A1 | 20000224 | WO 1999-JP4344 | 19990811 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| JP 2000119253 | A2 | 20000425 | JP 1999-226878 | 19990810 |
| CA 2340100 | AA | 20000224 | CA 1999-2340100 | 19990811 |
| AU 9951963 | A1 | 20000306 | AU 1999-51963 | 19990811 |
| EP 1104754 | A1 | 20010606 | EP 1999-937024 | 19990811 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2000143623 | A2 | 20000526 | JP 1999-242814 | 19990830 |
| US 6747023 | B1 | 20040608 | US 2001-762888 | 20010212 |
| US 2004082611 | A1 | 20040429 | US 2003-681205 | 20031009 |

PRIORITY APPLN. INFO.:
JP 1998-227449 A 19980811
JP 1998-244175 A 19980828
JP 1998-251674 A 19980904
WO 1999-JP4344 W 19990811
US 2001-762888 A3 20010212

OTHER SOURCE(S): MARPAT 132:194391

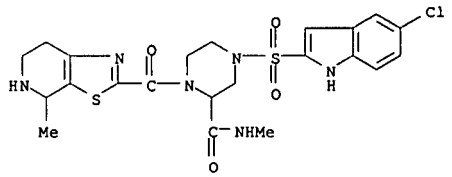
AB The title compds. Q1Q2T1Q3SO2QA [wherein Q1 is an optionally substituted, saturated or unsatd., five- or six-membered cyclic hydrocarbon group, a five- or six-membered heterocyclic group, or the like; Q2 is a single bond, oxygen, sulfur, C1-C6 alkylene or the like; Q3 is a heterocyclic ring (represented by several generic structures); QA is optionally substituted arylalkenyl, heteroarylalkenyl or the like; and T1 is carbonyl or the like] are prepared These compds. have potent factor Xa inhibiting effects and promptly exert satisfactory and persistent antithrombotic effects through oral administration, thus being useful as anticoagulant agents little accompanied with side effects. Several compds. of this invention in vitro showed IC50 values of 0.7 nM to 4.7 nM against factor Xa.

IT **259805-94-2P 259805-95-3P 259806-37-6P 259806-48-9P 259806-67-2P 259806-89-8P 259806-92-3P 259807-04-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl moiety-containing heterocyclic compds. as factor Xa inhibitors)

RN 259805-94-2 CAPLUS
CN 2-Piperazinecarboxamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-methyl-1-[(4,5,6,7-tetrahydro-4-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

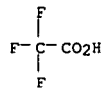
CM 1

CRN 259805-93-1
CMF C22 H25 Cl N6 O4 S2

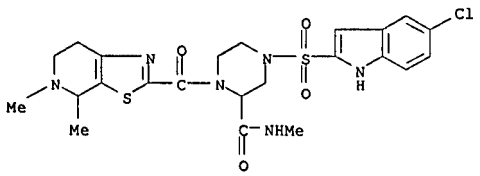


CM 2

CRN 76-05-1
CMF C2 H F3 O2

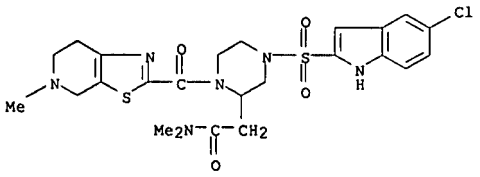


RN 259805-95-3 CAPLUS
CN 2-Piperazinecarboxamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-methyl-1-[(4,5,6,7-tetrahydro-4,5-dimethylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



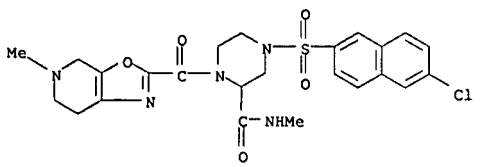
● HCl

RN 259806-37-6 CAPLUS
CN 2-Piperazineacetamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N,N-dimethyl-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

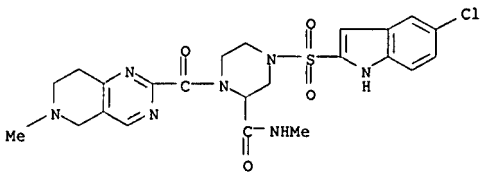


● HCl

RN 259806-48-9 CAPLUS
CN 2-Piperazinecarboxamide, 4-[(6-chloro-2-naphthalenyl)sulfonyl]-N-methyl-1-[(4,5,6,7-tetrahydro-5-methyloxazolo[5,4-c]pyridin-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

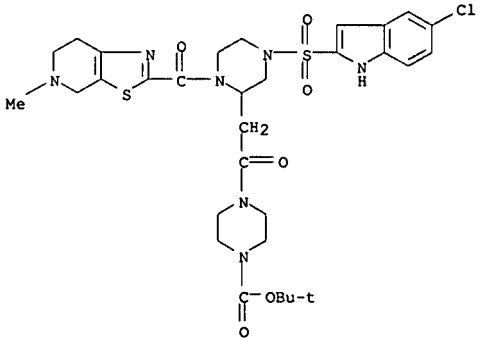


RN 259806-67-2 CAPLUS
CN 2-Piperazinecarboxamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-methyl-1-[(5,6,7,8-tetrahydro-6-methylpyrido[4,3-d]pyrimidin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

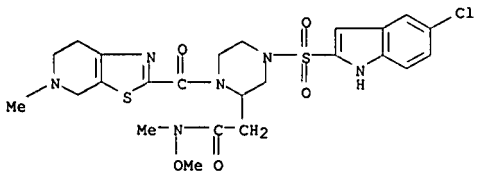


● HCl

RN 259806-89-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[(5-chloro-1H-indol-2-yl)sulfonyl]-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-2-piperazinyl]acetyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

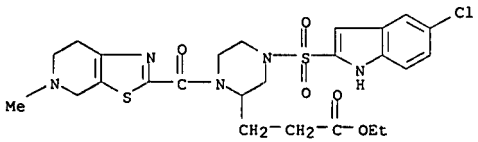


RN 259806-92-3 CAPLUS
CN 2-Piperazineacetamide, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-N-methoxy-N-methyl-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

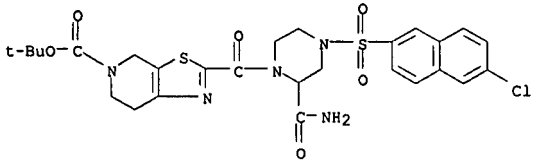


● HCl

RN 259807-04-0 CAPLUS
CN 2-Piperazinepropanoic acid, 4-[(5-chloro-1H-indol-2-yl)sulfonyl]-1-[(4,5,6,7-tetrahydro-5-methylthiazolo[5,4-c]pyridin-2-yl)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **222987-45-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonyl moiety-containing heterocyclic compds. as factor Xa inhibitors)
RN 222987-45-3 CAPLUS
CN Thiazolo[5,4-c]pyridine-5(4H)-carboxylic acid, 2-[[2-(aminocarbonyl)-4-[(6-chloro-2-naphthalenyl)sulfonyl]-1-piperazinyl]carbonyl]-6,7-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:487215 CAPLUS
DOCUMENT NUMBER: 131:130007
TITLE: Substituted piperazinone derivatives and other oxoazaheterocyclyl compounds useful as factor Xa inhibitors
INVENTOR(S): Ewing, William R.; Becker, Michael R.; Choi-Sledeski, Yong Mi; Pauls, Heinz W.; He, Wei; Condon, Stephen M.; Davis, Roderick S.; Hanney, Barbara A.; Spada, Alfred P.; Burns, Christopher J.; Jiang, John Z.; Li, Aiwen; Myers, Michael R.; Lau, Wan F.; Poli, Gregory B.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 300 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

102(e)

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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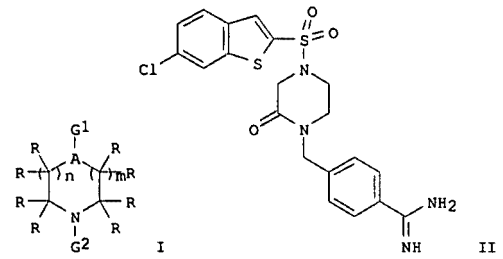
| WO 9937304 | A1 | 19990729 | WO 1999-US1682 | 19990127 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9900607 | A | 19990727 | ZA 1999-607 | 19990127 |
| CA 2319198 | AA | 19990729 | CA 1999-2319198 | 19990127 |
| AU 9926533 | A1 | 19990809 | AU 1999-26533 | 19990127 |
| AU 745425 | B2 | 20020321 | | |
| BR 9907300 | A | 20001024 | BR 1999-7300 | 19990127 |
| EP 1051176 | A1 | 20001115 | EP 1999-906684 | 19990127 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200002182 | T2 | 20001221 | TR 2000-200002182 | 19990127 |
| JP 2002501024 | T2 | 20020115 | JP 2000-528286 | 19990127 |
| EE 200000435 | A | 20020215 | EE 2000-435 | 19990127 |
| WO 2000032590 | A1 | 20000608 | WO 1999-US28074 | 19991124 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| JP 2003529531 | T2 | 20031007 | JP 2000-585232 | 19991124 |
| NO 2000003808 | A | 20000926 | NO 2000-3808 | 20000725 |
| BG 104633 | A | 20010330 | BG 2000-104633 | 20000725 |
| US 2004102450 | A1 | 20040527 | US 2003-628093 | 20030725 |
| PRIORITY APPLN. INFO.: | | | US 1998-72707P | A2 19980127 ← 102(e) |
| | | | US 1998-110012P | A2 19981125 |
| | | | WO 1999-US1682 | W 19990127 |
| | | | US 1999-313611 | A2 19990518 |
| | | | US 1999-363196 | A2 19990728 |
| | | | WO 1999-US28074 | W 19991124 |

OTHER SOURCE(S): MARPAT 131:130007
GI



I

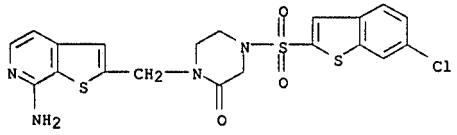


II

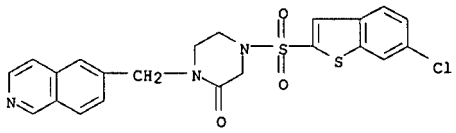
AB The invention is directed to oxoazaheterocyclyl compds. I and their pharmaceutically acceptable salts, prodrugs, N-oxides, hydrates, and solvates [wherein A = CH, N; G1, G2 = (independently) -L-Cy; L = various atomic and mol. linkers, including O, (un)substituted NH or S, alk(en/yn)ylene, etc., or their combinations; Cy = (un)substituted (hetero)aryl, cycloalk(en)yl, heterocyclyl, etc.; R = (independently) H, CO2H, alkoxycarbonyl, (un)substituted carbamoyl, alkyl, (hetero)aryl, (hetero)aralkyl; or two geminal R groups = O or S; m, n = 0-2; with provisos]. The compds. inhibit factor Xa (no data), and thereby the production of thrombin, and are thus useful as anticoagulants in the treatment of a wide variety of conditions. The invention is also directed to pharmaceutical compns., synthetic intermediates, and a method of inhibiting factor Xa. Examples include the synthesis of approx. 780 compds. I, which are also claimed, and several hundred intermediates. For instance, sulfonamidation of 6-chlorobenzo[b]thiophene-2-sulfonyl chloride with 4-(2-oxopiperazin-1-ylmethyl)benzamidine bistrifluoroacetate (prepns. given) in CH2Cl2 in the presence of Et3N gave title compound II.

IT **234099-55-9P 234099-62-8P 234100-32-4P 234100-58-4P 234105-43-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of piperazinone derivs. and other substituted oxoazaheterocyclyl compds. as factor Xa inhibitors)

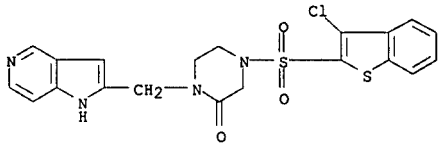
RN 234099-55-9 CAPLUS
CN Piperazinone, 1-[(7-aminothieno[2,3-c]pyridin-2-yl)methyl]-4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]- (9CI) (CA INDEX NAME)



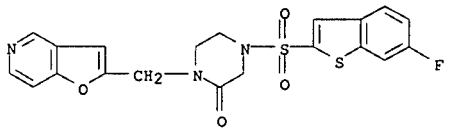
RN 234099-62-8 CAPLUS
CN Piperazinone, 4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-1-(6-isoquinolinylmethyl)- (9CI) (CA INDEX NAME)



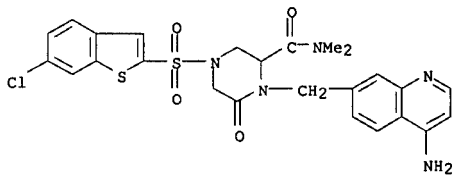
RN 234100-32-4 CAPLUS
CN Piperazinone, 4-[(3-chlorobenzo[b]thien-2-yl)sulfonyl]-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



RN 234100-58-4 CAPLUS
CN Piperazinone, 4-[(6-fluorobenzo[b]thien-2-yl)sulfonyl]-1-(furo[3,2-c]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



RN 234105-43-2 CAPLUS
CN 2-Piperazinecarboxamide, 1-[(4-amino-7-quinolinyl)methyl]-4-[(6-chlorobenzo[b]thien-2-yl)sulfonyl]-N,N-dimethyl-6-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:233901 CAPLUS
DOCUMENT NUMBER: 130:296694
TITLE: Preparation of heterocyclic compounds having the sulfonyl group as antithrombotics

INVENTOR(S): Kobayashi, Shozo; Komoriya, Satoshi; Ito, Masayuki; Nagata, Tsutomu; Mochizuki, Akiyoshi; Haginoya, Noriyasu; Nagahara, Takayasu; Horino, Haruhiko

PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

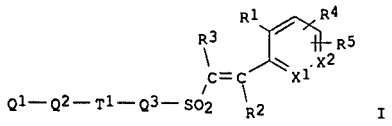
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9916747 | A1 | 19990408 | WO 1998-JP4411 | 19980930 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2304285 | AA | 19990408 | CA 1998-2304285 | 19980930 |
| AU 9892806 | A1 | 19990423 | AU 1998-92806 | 19980930 |
| EP 1031563 | A1 | 20000830 | EP 1998-945542 | 19980930 |
| EP 1031563 | B1 | 20051228 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| BR 9815377 | A | 20010116 | BR 1998-15377 | 19980930 |
| AT 314347 | E | 20060115 | AT 1998-945542 | 19980930 |
| US 6525042 | B1 | 20030225 | US 2000-508680 | 20000328 |
| NO 2000001636 | A | 20000329 | NO 2000-1636 | 20000329 |
| US 2003232808 | A1 | 20031218 | US 2002-323978 | 20021220 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| JP 1997-267117 | A | 19970930 |
| WO 1998-JP4411 | W | 19980930 |
| US 2000-508680 | A3 | 20000328 |

OTHER SOURCE(S): MARPAT 130:296694

GI



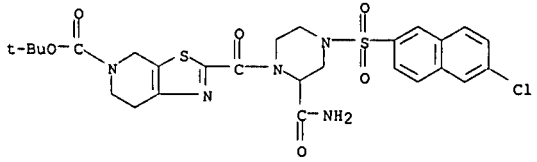
I


AB The title compds. I [R1 is hydrogen, hydroxyl, nitro or the like; R2 and R3 are each independently hydrogen, halogeno or the like; R4 and R5 are each independently hydrogen, halogeno or the like; Q1 is an optionally substituted saturated or unsatd. 5- or 6-membered cyclic hydrocarbon group or the like; Q2 is a single bond, oxygen or the like; Q3 is a heterocyclic moiety (represented by 4 generic structures); T1 is carbonyl or the like; and X1 and X2 are each independently methine or nitrogen] are prepared I speedily exert satisfactory and persistent antithrombotic effects through oral administration and cause few adverse effects. In an in vitro test for inhibition of activated blood coagulation factor X, 1-[(6-chloronaphthalen-2-yl)sulfonyl]-4-[(6-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]piperazine hydrochloride showed the Ki value of 6.6 nM.


IT **222987-45-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic compds. having the sulfonyl group as antithrombotics)

RN 222987-45-3 CAPLUS

CN Thiazolo[5,4-c]pyridine-5(4H)-carboxylic acid, 2-[[2-(aminocarbonyl)-4-[(6-chloro-2-naphthalenyl)sulfonyl]-1-piperazinyl]carbonyl]-6,7-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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